

B1
NO: 1). Analogous methods may be used to modulate conditions such as cell proliferation, cell differentiation, and cell death.

Please replace the 6th paragraph of page 5 with the following paragraph:

B2
Figure 5 illustrates amino acid sequences for the display of therapeutic polypeptide sequences in the Cys⁵³-Cys⁶² loop of mouse serum albumen. Sequences in the figure are represented by SEQ ID NOS. 6-11.

Please replace the 3rd paragraph of page 37 with the following paragraph:

B3
Myc epitope display in MSA loop regions. In order to determine whether the predicted loops were indeed exposed on the surface of the albumin molecule, mouse serum albumin (MSA) was modified to include the myc epitope, EQKLISEEDL (SEQ ID NO: 2). The myc epitope was inserted in the middle of each of three amino acid segments: between amino acids 57-58 for loop 53-62, amino acids 364-365 for loop 360-369 and amino acids 467-468 for loop 450-467. Cos7 cells were transfected with either wild type MSA or the various myc containing MSA constructs. The presence of the proteins in the medium was first determined by Western blot analysis using antibodies specific for MSA and the myc epitope. As can be seen in the left half of Figure 2, only samples from media from cells transfected with MSA or MSA-Myc reveal the presence of the albumin protein. Additionally, only the samples from cells transfected with MSA-Myc are positive for the myc epitope. As the samples are all denatured by virtue of the SDS-PAGE system, this analysis does not allow for the differentiation of myc epitopes that would be exposed on the surface versus one that was buried within the protein. For this analysis immunoprecipitation with the myc-specific antibody was utilized. In this experiment, the conditioned media was either mixed directly with the antibody (N, native) or first denatured in the presence of 0.1% SDS, 1 mM β -mercaptoethanol and heat (100 °C for 10 min) and then antibody added (D, denatured). Following immunoprecipitation the presence of the proteins that could be precipitated by the myc antibody were revealed by Western blot analysis using the MSA specific antibody. The right panel of Figure 2 shows that, as predicted, the albumin

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proteins with myc inserted in loops 53-62 and 360-369 were bound by the myc antibody regardless of whether the protein was in its native or denatured form. On the other hand, when myc was inserted in the predicted buried region, loop 450-463, the protein only bound the antibody when it was first denatured. This experiment clearly demonstrates that loops 53-62 and 360-369 are exposed on the surface of the MSA protein and therefore good for display.

Additionally, the 450-463 loop is buried.

B4

Please replace the 1st full paragraph of page 38 with the following paragraph:

Inhibition of bovine capillary endothelial cells (BCE) MSA-RGD. The goal of this experiment was determine the function of MSA with the RGD peptide (VRGDF, SEQ ID NO: 1) displayed on the surface of the protein in the loop 53-58 region (MSA-myc-RGD). RGD was chosen, as this peptide can efficiently bind to $\alpha\beta 3$ integrin receptors on endothelial cells and inhibit their proliferation. Triplicate wells of Cos7 cells were transfected with the following constructs: MSA-myc (the myc epitope was added to the C-terminal tail of MSA in this iteration); MSA-myc-RGD; or pAM7-stuffer. These Cos7 cells were grown in the lower chamber of a Transwell® tissue culture plate with BCE cells in the upper chamber. To stimulate growth of the BCE cells, FGF was added to the lower chamber or not in the case of no FGF control and the cells allowed to grow for 72 hours. To one set of wells, those with pAM7-stuffer, 6.25 μ M c-RGD peptide was also added. Cell growth was determined by a Calcein-binding fluorescence assay. The left panel of Figure 3 is a graph of the optical density (OD) for each. The data reveals the addition of FGF results in a 2-fold stimulation of growth of the BCE cells. This growth was inhibited by the c-RGD peptide and also by the secreted MSA-myc-RGD protein. The right panel is a different way of looking at the same data. In this instance the degree of inhibition of growth is graphed for each. The data shows that the MSA-Myc-RGD protein inhibited the growth of the BCE cell by 53% and the degree of inhibition was equivalent to that of the added RGD peptide. The RGD peptide displayed on the surface of the MSA molecule inhibited BCE cell growth as efficiently as the endogenously added free RGD peptide demonstrating that the peptide retains its activity in the looped orientation.

Please replace the last seven paragraphs of page 39 with the following paragraphs:

COS7-L cells were transfected with protein expression constructs expressing:

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1. MSA, full-length mouse serum albumin (negative control)
2. MSA-RGD, in which the RGD sequence (VRGDF, SEQ ID NO: 1) replaces the MSA sequence between Cys 53 and Cys 62
3. MSA-11B3, in which the 11-B3 peptide sequence (PSTLRAQ, SEQ ID NO: 3) replaces the MSA sequence between Cys 53 and Cys 62
4. MSA-1H5, in which the 1-H5 peptide sequence (HTKQIPRHIYSA, SEQ ID NO: 4) is inserted between Glu 57 and Ser 58 within the Cys 53 and Cys 62 loop of MSA
5. MSA-9G5, in which the 9-G5 peptide sequence (DSHKRLK, SEQ ID NO: 5) replaces the MSA sequence between Cys 53 and Cys 62
6. MSA-myc, in which the Myc epitope peptide sequence (EQKLISEEDL, SEQ ID NO: 2) is inserted between Glu 57 and Ser 58 within the Cys 53 and Cys 62 loop of MSA (negative control)

The paragraphs presented above incorporate changes as indicated by the marked-up versions below.

The 1st full paragraph of page 4:

The invention also comprises a pharmaceutical composition comprising a chimeric polypeptide as described above, and methods for treating a disease in an organism by administering an effective dose of such a pharmaceutical composition to the organism. In a currently preferred embodiment, a chimeric polypeptide according to the invention comprises a fragment of an angiogenesis-inhibiting protein, such as angiostatin or endostatin, as the heterologous peptide sequence and is capable of inhibiting angiogenesis. For example, a peptide fragment that inhibits angiogenesis and which may be incorporated into a subject polypeptide is RGD (Arg-Gly-Asp), or a sequence which includes the sequence RGD (e.g., VRGDF, SEQ ID NO: 1). Analogous methods may be used to modulate conditions such as cell proliferation, cell differentiation, and cell death.

The 6th paragraph of page 5:

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The 3rd paragraph of page 37:

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